

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (original) A method for introducing one or more mutations into a template double-stranded polynucleotide, wherein the template double-stranded polynucleotide has been cleaved into double-stranded random fragments of a desired size, comprising:
 - a) adding to the resultant population of double-stranded fragments one or more single or double-stranded oligonucleotides, wherein said oligonucleotides comprise an area of identity and an area of heterology to the template polynucleotide;
 - b) denaturing the resultant mixture of double-stranded random fragments and oligonucleotides into single-stranded fragments;
 - c) incubating the resultant population of single-stranded fragments with a polymerase under conditions which result in the annealing of said single-stranded fragments at regions of identity between the single-stranded fragments and formation of a mutagenized double-stranded polynucleotide; and
 - d) repeating steps (b) and (c).
2. (original) The method of Claim 1 wherein the concentration of a specific double-stranded fragment in the mixture of double-stranded fragments is less than 1% by weight of the total DNA.
3. (original) The method of Claim 1 wherein the number of different specific double-stranded fragments comprises at least about 100.
4. (original) The method of Claim 1 wherein the size of the double-stranded fragments is from about 5 bp to 5 kb.
5. (original) The method of Claim 1 wherein the size of the mutagenized double-stranded polynucleotide comprises from 50 bp to 100 kb.

6. (original) A method of producing recombinant proteins having biological activity comprising:

- a) treating a sample comprising double-stranded template polynucleotides encoding a wild-type protein under conditions which provide for the cleavage of said template polynucleotides into random double-stranded fragments having a desired size;
- b) adding to the resultant population of random fragments one or more single or double-stranded oligonucleotides, wherein said oligonucleotides comprise areas of identity and areas of heterology to the template polynucleotide;
- c) denaturing the resultant mixture of double-stranded random fragments and oligonucleotides into single-stranded fragments;
- d) incubating the resultant population of single-stranded fragments with a polymerase under conditions which result in the annealing of said single-stranded fragments at the areas of identity and formation of a mutagenized double-stranded polynucleotide;
- e) repeating steps (c) and (d); and
- f) expressing the recombinant protein from the mutagenized double-stranded polynucleotide.

7. (original) The method of Claim 6 wherein the concentration of a specific double-stranded fragment in the mixture of double-stranded fragments in step (a) is less than 1% by weight of the total DNA.

8. (original) The method of Claim 6 where the number of different specific double-stranded fragments in step (a) comprises at least about 100.

9. (original) The method of Claim 6 wherein the size of the double-stranded fragments is from about 5 bp to 5 kb.

10. (original) The method of Claim 6 wherein the size of the mutagenized double-stranded polynucleotide comprises from 50 bp to 100 kb.

11. (original) The method of Claim 6 further comprising selecting the desired recombinant protein from the population of recombinant proteins.

12. (original) A method for obtaining a chimeric polynucleotide comprising:
 - a) treating a sample comprising different double-stranded template polynucleotides wherein said different template polynucleotides contain areas of identity and areas of heterology under conditions which provide for the cleavage of said template polynucleotides into random double-stranded fragments of a desired size;
 - b) denaturing the resultant random double-stranded template fragments contained in the treated sample produced by step (a) into single-stranded fragments;
 - c) incubating the resultant single-stranded fragments with polymerase under conditions which provide for the annealing of the target single-stranded fragments at the areas of identity and the formation of a chimeric double-stranded polynucleotide sequence comprising template polynucleotide sequences; and
 - d) repeating steps (b) and (c) as desired.
13. (original) The method of Claim 12 wherein the concentration of a specific double-stranded fragment in the mixture of double-stranded fragments in step (a) is less than 1% by weight of the total DNA.
14. (original) The method of Claim 12 where the number of different specific double-stranded fragments in step (a) comprises at least about 100.
15. (original) The method of Claim 12 wherein the size of the double-stranded fragments is from about 5 bp to 5 kb.
16. (original) The method of Claim 12 wherein the size of the mutagenized double-stranded polynucleotide comprises from 50 bp to 100 kb.

Claims 17-32 (cancelled)